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ORIGINAL ARTICLE

Synthesis, conformational studies and inclusion properties of N-substituted tetrahomodiazacalix[4]arenes

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Abstract A series of tetrahomodiazacalix[4]arenes (**1–8**) with different substituents (or substituted) at the upper rim and/or *N*-side arm has been synthesized with acceptable yields. The compounds were characterized by elemental analysis, IR, MS and NMR methods. In particular, **5** was shown by X-ray crystallography to adopt the cone conformation in the solid state. Two-phase picrate extraction showed that **2** and **6**, bearing *N*-2-picolyl arms, are the best extractants. Of the cations tested, Ag(I) is the best extracted by almost all ligands and the extraction efficiency follows the order 2-picolyl > 3-picolyl > 4-picolyl.

Keywords Supramolecular chemistry · Tetrahomodiazacalix[4]arenes · Cation complexation

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Introduction

The base-induced condensation of *p*-substituted phenols and formaldehyde produces the calixarenes, macrocyclic compounds available in a variety of ring sizes, which constitute highly attractive platforms for the synthesis of more elaborate host molecules by chemical modification [1]. This is an effective and versatile way of producing receptors with highly selective cation binding properties [1]. Even minor changes in the functionalization or conformation of chemically modified calixarenes can lead to drastic changes in the complexation behaviour [1]. Although most modifications have involved the phenolic rings, they have also concerned the methylene groups which serve to link the phenolic units into a macrocyclic structure: they have been replaced by $(CH_2)_n$ to give homocalixarenes analogues [2], by CH_2OCH_2 to give homooxacalixarenes [3], by S atoms to give thiacalixarenes [4], and more recently by CH_2SCH_2 to give homothiacalixarenes [5]. As well, the name homoazacalixarene (or azacalixarene) is currently used to designate calixarene analogues in which the CH_2 groups are partly or completely replaced by CH_2NRCH_2 [6, 7]. The presence of a soft nitrogen atom in azacalixarenes might be expected to change their metal-ion-binding characteristics [7c] as well as to offer new ways of modifying the overall structure. In 1992, Takemura et al. [7a] described the synthesis of *N*-benzyl-hexa-homotriaza-*p*-methylcalix[3]arene from the reaction between 2,6-bis(hydroxymethyl)-4-methylphenol and benzylamine. Subsequently, the same group [7b] described the synthesis and conformational properties of *N*-benzyl-tetra-homodiaza-*p*-*tert*-butylcalix[4]arene (**5**) (see Chart 1, R = *tert*-butyl,

R' = phenyl). **5** was demonstrated by variable temperature ^{1}H NMR to adopt a cone conformation over a wide range of temperature in various solvents while Thuéry et al. [7g, h, j] reported that the related *N*-benzyl-tetra-homodiaza-*p*-methylcalix[4]arene (R = methyl; R' = phenyl) is in a twisted cone conformation in the crystal state.

X-ray structure determinations have shown that the coordination of *N*-benzyl-tetra-homodiaza-*p*-methylcalix[4]arene (R = methyl; R' = phenyl) to ytterbium(III) [7h] or uranyl ion [7j, k] gives 1:1 complexes in which the metal ions are bound only to phenoxide donors of the macrocycle in addition (in some cases) to simple anions. The form of the complex can, however, be strongly influenced by the state of protonation of the zwitterionic ligand, passing, in the case of uranyl ion, from the situation where the metal is located ''internally'' by the macrocycle to another where it is ''externally'' bound. Hydrogen-bonding involving the N-centres appears to be a significant influence upon the rather flattened cone conformation of the ligand in its complexes.

The synthesis known for tetra-homodiazacalix[4]arenes is useful because it allows the introduction of *N*-side arms with functionality [7b, d, f–h, j–l]. While tetra-homodiazacalix[4]arenes **(1)** [7d, l] and **(5)** [7b] result from reacting the corresponding *o*,*o*'-bis(hydroxymethyl) *p*-substituted phenol dimer with benzylamine, replacing the benzylamine by an alkylamine bearing a special function may lead to more sophisticated molecular receptors. Mention has been made of such syntheses of *N*-substituted-tetra-homodiaza-*p*-methylcalix[4]arenes [6a] but no experimental data has been published and the reaction products were described simply as viscous oils which were not further characterised.

In this paper we report the synthesis and a preliminary study of the metal-binding properties of tetrahomodiazacalix[4]arenes **1–8** (see Chart 1), diversely substituted on the upper rim (R = phenyl or *tert*-butyl) and/or the *N*-side arm (R' = benzyl, 2-picolyl, 3-picolyl and 4-picolyl). The choice of the picolyl residue comes from the observation of Pappalardo et al. [8] and Danil de Namor et al. [9] that so-called pyridino calixarenes having pendant pyridine groups at the lower rim are good N-donor ligands for transition metal ions. Similarly, Yamato et al. [10] reported that homocalixarenes bearing pyridyl moieties were able to chelate Ag(I), with a binding selectivity depending on the position of the N-atom in the picolyl group.

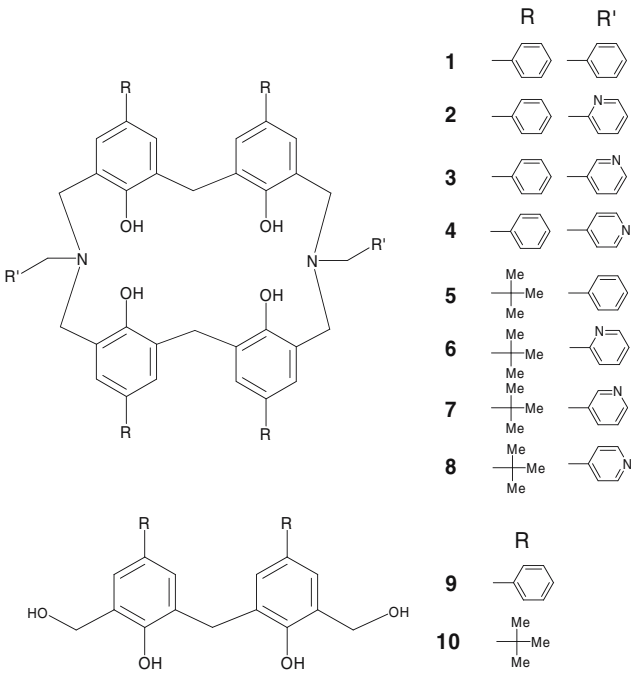

Chart 1 Tetrahomodiazacalix[4]arenes **1–8** and their corresponding dimer precursors **9** and **10**

Results and discussion

Synthesis of azacalixarenes **2–4** and **6–8**

Azacalixarenes **1** [7d, l] and **5** [7b] were prepared using the literature method. A similar procedure was used to prepare azacalixarenes **2–4** and **6–8** by heating 2,2'-bis (hydroxymethyl) *p*-substituted phenol dimers **9** [7d, l] (R = phenyl) and **10** [7b](R = *tert*-butyl) with 2-, 3- and 4-picolylamines, respectively, in xylene at reflux for 20 h, with azeotropic removal of water. Azacalixarenes **2–4** precipitated in the reaction mixture during the work up while **6–8** were crystallized from methylene chloride (solvent) and methanol (non-solvent). These moderately high-melting (~120–220°C) solids were obtained in acceptable yields (37–65%). Mass spectra and microanalyses were in good agreement with the proposed structures. The high symmetry of the cyclic products was apparent from their ^{1}H and ^{13}C NMR spectra. For instance, four broad singlets were detected at 4.30, 3.74, 3.64 and 3.48 ppm for the methylene CH_2 protons and only one singlet at 1.27 ppm for the *tert*-butyl groups in the ^{1}H NMR spectrum of **7**. In the ^{13}C spectrum, NCH_2Py appears as a single signal at 58.97 ppm. Similar findings were made for azacalixarenes **6–8** bearing *tert*-butyl groups. Although in some cases the methylene-bridge protons

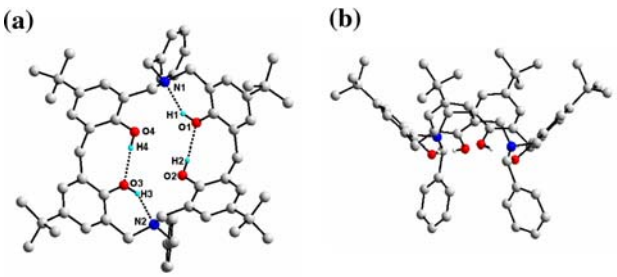

Fig. 1 Projections of the molecular unit found in the lattice of **5**•($C_2H_5OC(=O)CH_3$) ((**a**) top-, and (**b**) side-view),with intramolecular hydrogen bonding interactions shown as dotted lines. Non-phenolic hydrogen atoms are omitted for clarity

appeared as broad doublets, consistent with a slowing of conformational changes possibly as a consequence of phenolic group H-bonding interactions, in general these azacalixarenes appear to be conformationally labile at room temperature.

X-ray crystallography

Crystallographic data for **5** have been deposited with the Cambridge Crystallographic Database, CCDC reference number 612313. Data $C_{64}H_{82}N_2O_6$; M = 975.32; monoclinic $P2_1/c$; a = 16.2968(11)Å; b =17.1132(11) Å; c = 22.2781(14) Å; β = 108.064(2); V = 5906.9(7) Å^3; T = 293(2) K; Z = 4; l = 0.069 mm^{-1}; 13785 reflections; R_{int} = 0.0597; $R_1[F^2 > 2\sigma(F^2)]$ = 0.0626; $wR_2(F^2)$ = 0.1666.

A yellow plate single crystal of **5**·(EtOAc) was obtained from a mixed solution (EtOAc/CH_2Cl_2) at 20°C. The azacalixarene molecule (Fig. 1) has a C_{2v}-symmetry (''pinched cone'') conformation with the four hydroxyl (OH) groups oriented in the same direction. One highly disordered ethyl acetate molecule is located within the shallow cavity defined by the calixarene. The aza-group nitrogen atoms N(1) and N(2) are pyramidal, with mean C-N-C angles of 110.0° and 110.8°, respectively. Parameters defining the intramolecular H-bonds are given in Table 1.

Table 1 Structure data of hydrogen bonding interactions in **5**

Donor-H ···Acceptor	D-H(Å)[a]	H···A(Å)	D···A(Å)	∠(D-H···A) (°)
O1-H1···N1	0.82	1.96	2.6870	148
O2-H2···O1	0.82	1.99	2.8097	175
O3-H3···N2	0.82	1.96	2.6850	148
O4-H4···O3	0.82	1.92	2.7380	176

[a] Fixed distance and calculated position

The presence of OH...N...HO units seems to be general, since it has been seen in all known tetra-homodiazacalix[4]arene structures [7f, i]. Infra-red spectroscopy also provides evidence for such intramolecular hydrogen-bonds [7b].

Two-phase extraction

To obtain insight into possible applications of the coordination chemistry of ligands **1**–**8**, we examined their use in solvent extraction of several metal ions. For Na^+, K^+, Rb^+, Cs^+, NH_4^+, Ag^+, Sr^{2+}, Ba^{2+} and Pb^{2+} as their picrates in the system water/1,2-dichloroethane, some preliminary data are given in Table 2.

Overall, ligands **5**–**8** are more effective extractants than ligands **1**–**4**. This presumably reflects the presence of the *tert*-butyl substituent and its influence on the lipophilicity of the complexes and perhaps upon their stability. Ligands **2** and **6**, bearing *N*-2-picolyl arms, are particularly efficient extractants, **6** being the most effective. A similar enhancement (~50–60 times) has been observed on substituting *N*-2-picolyl-hexa-homotriaza-*p*-methylcalix[3]arene for its *N*-benzyl analogue in the extraction of alkali-metal picrates [10]. Extraction of Ag(I) is generally very efficient under the given conditions except for the ligands **1** and **5**, which are those with a simple *N*-benzyl substituent lacking extra *N*-donor centres. This suggests that the coordination of Ag(I) to the pendent-arm *N*-centres is especially important in its extraction.

Association constants

As the most efficiently extracted species, Ag(I) was chosen for assessment of association constants and free energies. First, titrations of AgPic with the ligands **1**–**8** were carried out to determine the stoichiometry of the complexes. The results showed a 2:1 (Ag^+:ligand) ratio. Association constants (K_a) and free energies (ΔG^0) were calculated and listed in Table 3. The K_a and ΔG^0 values are defined by the equations:

$$2[Ag^+Pic^-]_0 + [H]_0 \overset{K_a}{\rightleftharpoons} [(Ag^+Pic^-)_2H]_0 \quad (1)$$

$$2[Ag^+]_{aq} + 2[Pic^-]_{aq} + [H]_0 \overset{K_{ex}}{\rightleftharpoons} [(Ag^+Pic^-)_2H]_0 \quad (2)$$

$$[Ag^+]_{aq} + [Pic^-]_{aq} \overset{K_d}{\rightleftharpoons} [Ag^+Pic^-]_0 \quad (3)$$

$$K_a = K_{ex} / K_d^2 \quad (4)$$

Table 2 Extraction of metal picrates by ligands **1–8**[a]

Ligands	Percentage extraction								
	Na^+	K^+	Rb^+	Cs^+	NH_4^+	Ag^+	Sr^{2+}	Ba^{2+}	Pb^{2+}
1	9.6	7.1	10.0	7.3	7.6	12.5	5.9	5.7	5.3
2	**25.1**	**13.9**	**25.6**	**7.7**	**16.8**	**62.9**	**15. 6**	**14.9**	**6.6**
3	13.6	11.7	16.5	9.0	11.5	57.4	9.1	8.1	21.7
4	11.5	8.8	14.3	7.4	9.4	50.2	7.7	6.9	11.6
5	19.7	17.8	25.5	10.7	18.9	29.9	15.9	12.0	4.5
6	**46.9**	**47.3**	**50.5**	**35.9**	**48.3**	**59.3**	**32.9**	**29.1**	**25.5**
7	12.9	9.1	17.2	7.0	10.0	64.4	8.59	7.6	24.5
8	12.3	7.6	15.6	6.1	8.5	58.9	8.10	6.5	16.5

[a] Conditions: ligand, 0.1 mM/$ClCH_2CH_2Cl$; metal picrate, 0.2 mM/water. Picrate concentrations in the aqueous phase were determined by measurement of visible absorption spectra

Table 3 Association constants and free energies of complexation of silver picrate by **1–8** at 25°C. All errors ± 10%

Compound	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
$\log K_a$ (M^{-2})	19.32	21.83	21.50	21.12	20.17	21.62	21.93	21.56
$-\Delta G^0$ (kcal/mol)	26.34	29.77	29.32	28.80	27.50	29.47	29.90	29.44

Table 3 exhibits the trends of extraction data in which the best $\log K_a$ and ΔG^0 were found for the ligands bearing picolyl residues. As expected due to the absence of N atoms in the N-aromatic ring, ligands **1** and **5** were observed to give the smallest values. No striking effects were seen of the position of the nitrogen atom on the pyridine ring.

^{1}H NMR and mass spectrometry studies

^{1}H NMR has been often used to give information on the stoichiometry of the complexes, the mode of complexation of cations, and more particularly of the location of the cation in a macrocycle during the formation of a complex. Extended reaction (until the spectra remain the same) of ~10^{-2} M $CDCl_3$ solutions of **5–8** (the extraction data and thermodynamics being almost the same in the series of ligands, only these were investigated as a model) with an excess solid AgPic, followed by filtration results in the formation of species of 2:1 stoichiometry for ligands **5** and **6** and 1:1 for **7** and **8** (as judged by integration of the ^{1}H NMR spectrum). The difference with the results of the association constants can be due to the fact that extraction data reflect the solubility of the complexes and the reactant picrate while the association constants are determined in homogeneous systems. In the case of ligand **5** one can assume the formation of 2:1 complexes with chelation of Ag(I) near of the N atom in the macrocycle. For ligand **6**, a similar mode of complexation occurs with the assistance of the N-pyridine atom in a favourable position leading to a stronger

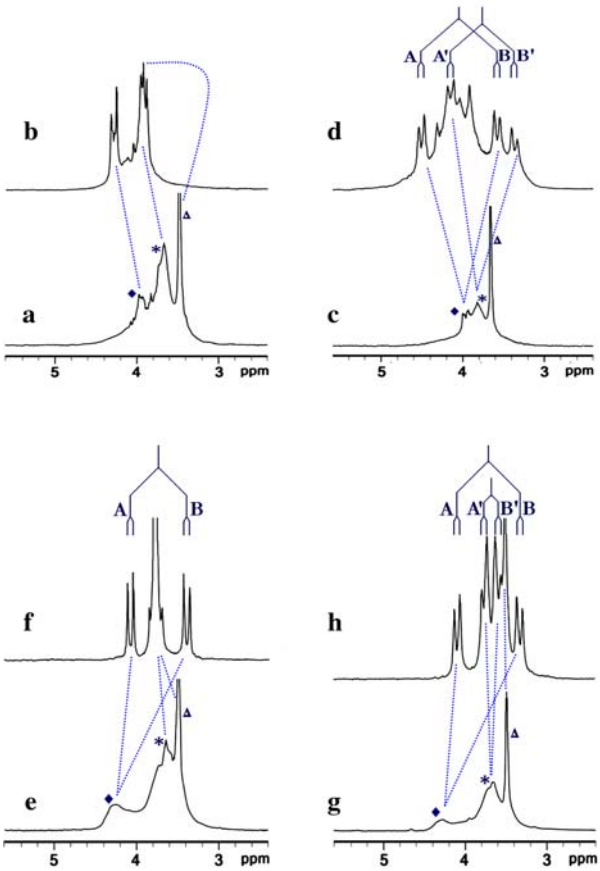

Fig. 2 ^{1}H-NMR spectra of the ligands **5–8** and their Ag(I) complexes (**a, b**: ligand **5** and its complex, respectively; **c, d**: ligand **6** and its complex, respectively; **e**, **f**: ligand **7** and its complex, respectively; **g, h**: ligand **8** and its complex, respectively; ♦: ArCH_2Ar; *: NCH_2Ar; Δ: NCH_2Py)

complex. When the N-pyridine atom is 3- or 4-picolyl type, this chelation mode is no longer possible and another complexation mode leads to the formation of 1:1 species.

Figure 2 gives the region corresponding to the ArCH_2Ar, NCH_2Ar and NCH_2R' of ^{1}H-NMR spectra of the ligands **5–8** and their Ag(I) complexes. For ligand **5** (Fig. 2a and b) no drastic changes are observed while significant changes in the ligands **6–8** spectra resulting from complexation are most readily discerned in the well-resolved resonance signals, displaying several AB systems. A rigidification of ligands **6–8** can be deduced from the appearance of these AB systems. This was also in agreement with the formation of a weaker complex of **5** with Ag (I). Although the different signals could be attributed, no conformation has been assigned to the azacalixarene macrorings. The rigidification corresponding to the azacalixarene ring we can assume the N atoms of the macroring to be involved in the complexation process.

The ^{1}H NMR solutions were directly used for mass spectrometry. Only could be detected the mono- and binuclear complexes of ligand **6** with Ag(I) also in agreement with a better complexation with 2-pycolyl moiety. The mass spectrum presented peaks at *m/z* = 889.52 corresponding to the free ligand (MW_{calcd} = 888.56), *m/z* = 1023.15 corresponding to **6**·Ag·Na + 3H (MW_{calcd} for **6** + Ag = 997.08) and *m/z* = 1100.20 corresponding to **6**·2Ag–2H (MW_{calcd} for **6** + 2Ag = 1102.37).

Conclusions

Tetra-homodiazacalix[4]arenes **(1–8)** diversely substituted at the upper rim (R = phenyl or *tert*-butyl) and/or the *N*-side arm (R' = benzyl, 2-picolyl, 3-picolyl and 4-picolyl) were prepared in reasonable yields. The various macrocycles were shown to be flexible in solution, presenting no preferential conformation. In the solid state, one of them, **5** was shown to adopt the cone conformation. From extraction and thermodynamical data, the ligands bearing *N*-picolyl residues were observed to be better extractants of metal cations than the corresponding *N*-benzyl ones due to the presence of a chelating *N* atom in the pyridine ring. The best complexed cation is the silver. The position of the *N* atom in the pyridine was shown to lead to better complexes with silver. In the presence of silver, the ligands bearing picolyl residues rigidified but the conformation of the macrocycle in the complexes could not be assumed on the view of the ^{1}H NMR data. The involvement of the *N*-picolyl nitrogen atom may lead to the formation of endo (in which both silver atoms are inside the azacalixarene) and/or exo (in which the silver cation may serve as a linker between at least two azacalixarenes) complexes. Such assumptions are currently under investigations.

Experimental section

Materials and analytical procedures

Unless otherwise noted, reagents were obtained from commercial suppliers and used without further purification. Melting points were taken in evacuated and sealed capillary tubes with a Mel-Temp apparatus and were uncorrected. IR spectra were recorded on a Nicolet Impact 400 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Varian 200 MHz spectrometer in Dankook University. Chemical shifts are given in parts per million (ppm) relative to TMS as an internal standard. Mass spectrometry MALDI TOF spectra were recorded on a Voyager-DE^{TM} STR Bio-spectrometry_Workstation made by Applied Biosystems Inc. Azacalixarenes **1** [7d, l] and **5** [7b] and *o*,*o*'-bis(hydroxymethyl) *p*-substituted phenol dimers **9** [7d, l] and **10** [7b] were prepared according to literature.

Picrate extraction experiments

The percentages of cation picrates extracted from water to 1,2-dichloroethane have been determined at 20°C according to the Pedersen's procedure [11]. 5 ml of aqueous solutions of cation picrates (0.2 mM) were shaken as two-phase systems with 5 ml of a solution of ligands (0.1 mM) in 1,2-dichloroethane. This was repeated three times, the solutions being stored until phase separation was complete. The extractability was determined spectrophotometrically from the decrease in the absorbance of the picrate ion at λ = 373 nm in the aqueous phase.

Preparation of azacalixarenes **2–4** and **6–8**

N,N-Di(2-picolyl)-7,13,21,27-tetra-phenyl-29,30,31,32-tetrahydroxy-2,4,16,18-tetra-homo-3,17-diazacalix[4]arene (2)

A solution of **9** (2.47 g, 5.99 mmol) and 2-picolylamine (1.6 ml, 15.5 mmol) in 80 ml of xylene was refluxed for 20 h using a Dean-Stark to remove water. After partial removal of solvents under reduced pressure, the reaction mixture was cooled to room temperature. A precipitate was formed which was isolated to afford 1.59 g (55%) of pure product **2** as pale yellow crystals.

Mp 127–128°C. IR (KBr pellet, cm^{-1}): 3462, 1219. ^1H NMR (DMSOd_6) δ 8.61 (d, 2H, PyH_6, J = 4.2 Hz), 7.81(d of t, 2H, PyH_5, J = 7.6 & 1.6 Hz), 7.53 (t, 4H, PyH_4, J = 1.6 Hz), 7.51 (t, 4H, ArH, J = 1.0 Hz), 7.48 (d, 2H, PyH_3, J = 2.4 Hz), 7.43–7.34 (m, 16H, ArH), 7.25–7.19 (m, 6H, ArH), 5.30 (bs, 4H, OH), 4.58, 4.10, 4.07 (3s, 12H, ArCH_2), 3.93 (s, 4H, NCH_2Py); ^{13}C NMR (DMSOd_6) δ 160.14, 156.34, 153.93, 149.74, 141.54, 141.32, 137.64, 130.68, 130.10, 129.63, 129.38, 129.36, 129.25, 128.28, 127.38, 126.70, 126.53, 126.44, 126.29, 125.90, 123.95, 123.52, 123.27, 121.35 (Ar & Py), 60.14, 51.85, **51.28** (NCH_2Py), 32.10 (ArCH_2Ar). FAB^+ (MS): m/z = 1009.89 $(M + K)^+$ (MW_{calcd} = 969.18). Anal. Calcd for $C_{66}H_{56}N_4O_4$: C, 81.80; H, 5.82. Found: C, 82.01; H, 5.85.

N,N-Di(3-picolyl)-7,13,21,27-tetra-phenyl-29,30,31,32-tetrahydroxy-2,4,16,18-tetra-homo-3,17-diazacalix[4]arene (3)

In similar conditions, the reaction of **9** and 3-picolylamine produced **3** (1.75 g, 60%) as pale yellow crystals. Mp 217–218°C; IR (KBr pellet, cm^{-1}): 3380, 1211. Mp 217–218°C; ^1H NMR ($CDCl_3$) δ 10.86, 8.63, 8.57 (3bs, 4H, OH), 7.86–6.96 (m, 36H, PyH & ArH), 4.42 (bs, 4H, NCH_2Py), 3.88 (bd, 2H, J = 14.4 Hz, ArCH_2Ar), 3.76 (bd, 2H, J = 14.4 Hz, ArCH_2Ar), 3.64, 3.55 (2 bs, 8H, NCH_2Ar); ^{13}C NMR ($CDCl_3$) δ 151.03, 140.93, 133.70, 129.78, 129.10, 128.94, 128.17, 126.99, 126.93, 126.22, 125.98 (Ar & Py), 63.34, **58.77** (NCH_2Py), 34.08 (ArCH_2Ar). FAB^+ (MS): m/z = 969.23 $(M)^+$ (MW_{calcd} = 969.18). Anal. Calcd for $C_{66}H_{56}N_4O_4$: C, 81.80; H, 5.82. Found: C, 81.89; H, 5.79.

N,N-Di(4-picolyl)-7,13,21,27-tetra-phenyl-29,30,31,32-tetrahydroxy-2,4,16,18-tetra-homo-3,17-diazacalix[4]arene (4)

In similar conditions, the reaction of **9** and 4-picolylamine produced **4** (1.48 g, 51%) as pale yellow crystals. Mp 223–224°C; IR (KBr pellet, cm^{-1}): 3450, 1210. ^1H NMR ($CDCl_3$) δ 10.76 (bs, 1H, OH), 8.65 (bs, 3H, OH), 7.52–6.96 (m, 36H, ArH & PyH), 4.44 (bs, 4H, NCH_2Py), 3.89 (bd, 2H, J = 10.8 Hz, ArCH_2Ar), 3.76 (bs, 4H, NCH_2Ar), 3.64 (bd, 2H, J = 10.8 Hz, ArCH_2-Ar), 3.57 (bs, 4H, NCH_2Ar); ^{13}C NMR ($CDCl_3$) δ 140.87, 133.80, 129.28, 129.10, 128.94, 128.15, 126.98, 126.22, 124.59, 122.88 (Ar & Py), **58.90** (NCH_2Py), 33.85 (ArCH_2Ar). FAB^+ (MS) : m/z = 969.21 $(M)^+$ (MW_{calcd} = 969.18). Anal. Calcd for $C_{66}H_{56}N_4O_4$: C, 81.80; H, 5.82. Found: C, 81.95; H, 5.78.

N,N-Di(2-picolyl)-7,13,21,27-tetra-tert-butyl-29,30,31,32-tetrahydroxy-2,4,16,18-tetra-homo-3,17-diazacalix[4]arene (6)

A solution of **10** (2.23 g, 5.99 mmol) and 2-picolylamine (1.2 ml, 11.6 mmol) in 80 ml of xylene was heated under reflux for 20 h using a Dean-Stark to remove water. After removal of solvent under reduced pressure, recrystallization of the reaction mixture from methylene chloride and methanol gave 1.21 g (46%) of **6** as pale yellow crystals. Mp 150–151°C; IR (KBr pellet, cm^{-1}): 3451, 1210. ^1H NMR ($CDCl_3$) δ 10.61 (bs, 4H, OH), 8.56 (bs, 1H, PyH_6), 7.61 (bs, 1H, PyH_5), 7.21 (bs, 8H, ArH), 6.85 (2 bs, 6H, ArH + PyH_{3+4}), 4.34–3.64 (bm, 16H, NCH_2Py & ArCH_2), 1.25 (s, 36H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 151.45, 142.45, 136.81, 127.53, 126.94, 125.61, 123.99, 122.48, 122.12 (Ar & Py), **60.42** (NCH_2Py), 34.07 (C(CH_3)$_3$), 31.75 (C(CH$_3$)$_3$). 31.41 (ArCH_2Ar). Found: C, 78.28; H, 8.35.FAB^+ (MS) : m/z = 887.15 $(M)^+$ (MW_{calcd} = 887.24). Anal. Calcd for $C_{58}H_{72}N_4O_4$: C, 78.34; H, 8.16. Found: C, 78.28; H, 8.35.

N,N-Di(3-picolyl)-7,13,21,27-tetra-tert-butyl-29,30,31,32-tetrahydroxy-2,4,16,18-tetra-homo-3,17-diazacalix[4]arene (7)

In similar conditions reaction of **10** and 3-picolylamine afforded 1.73 g (65%) of **7** as pale yellow crystals. Mp 230–233°C; IR (KBr pellet, cm^{-1}): 3450, 1212. Mp 230–223°C; ^1H NMR ($CDCl_3$) δ 10.82, 10.49 (2 bs, 4H, OH), 8.55, 7.85, 7.52, 7.38, 6.88 (5 bs, 16H, ArH & PyH), 4.30, 3.74, 3.64, 3.48 (4 bs, 16H, NCH_2Py & ArCH_2), 1.27 (s, 36H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 151.03, 148.93, 142.71, 137.56, 133.64, 127.62, 127.06, 125.71, 121.95 (Ar & Py), **58.97** (NCH_2Py), 34.11 (C(CH_3)$_3$), 31.76 (C(CH$_3$)$_3$ & ArCH_2Ar). FAB^+ (MS): m/z = 889.17 (MW_{calcd} = 889.22). Anal. Calcd for $C_{58}H_{72}N_4O_4$: C, 78.34; H, 8.16. Found: C, 78.21; H, 8.25.

N,N-Di(4-picolyl)-7,13,21,27-tetra-tert-butyl-29,30,31,32-tetrahydroxy-2,4,16,18-tetra-homo-3,17-diazacalix[4]arene (8)

In similar conditions, **10** and 4-picolylamine afforded 993 mg (37%) of **8** as pale yellow crystals. Mp 222–223°C; IR (KBr pellet, cm^{-1}): 3450, 1199. ^1H NMR ($CDCl_3$) δ 10.42 (bs, 4H, OH), 8.60, 7.35, 7.26, 6.87 (4 bs, 16H, ArH & PyH), 4.31, 3.73, 3.63, 3.48 (4 bs, 16H, NCH_2Py & ArCH_2), 1.27 (s, 36, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 150.98, 150.14, 142.83, 127.61, 127.15,

125.72, 124.65, 121.91 (Ar & Py), **59.90** (NCH_2Py), 34.10 ($C(CH_3)_3$), 31.73 ($C(CH_3)_3$), 31.70 ($ArCH_2Ar$). FAB^+ (MS): m/z = 889.21 $(M)^+$ (MW_{calcd} = 889.22). Anal. Calcd for $C_{58}H_{72}N_4O_4$: C, 78.34; H, 8.16. Found: C, 78.21; H, 8.31.

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